

SEQUENCE LISTING

<110> Conaris Research Institute GmbH

<120> Diagnostic Use of Polymorphisms in the Gene Coding for
the TNF Receptor II and Method for Detecting
Non-Responders to Anti-TNF-Therapy

<130> K51347/8

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<170> PatentIn Ver. 2:1

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<223> Description of Artificial Sequence: Forward Primer

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<223> Description of Artificial Sequence: Forward Primer

09902175.071001

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agcctggaca acatggcga

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09902175-071001

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0990217E-071001

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00902476-071001

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21

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26

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26

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20

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15

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Met Ala Pro Val Ala Val Trp Ala
-20 -15

gcg ctg gcc gtc gga ctg gag ctc tgg gct gcg gcg cac gcc ttg ccc 161
Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro
-10 -5 -1 1

gcc cag gtg gca ttt aca ccc tac gcc ccg gag ccc ggg agc aca tgc 209
Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys
5 10 15

cgg ctc aga gaa tac tat gac cag aca gct cag atg tgc tgc agc aaa 257
Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
20 25 30

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| Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp | |
| 35 40 45 50 | |
| acc gtg tgt gac tcc tgt gag gac agc aca tac acc cag ctc tgg aac | 353 |
| Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn | |
| 55 60 65 | |
| tgg gtt ccc gag tgc ttg agc tgt ggc tcc cgc tgt agc tct gac cag | 401 |
| Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln | |
| 70 75 80 | |
| gtg gaa act caa gcc tgc act cgg gaa cag aac cgc atc tgc acc tgc | 449 |
| Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys | |
| 85 90 95 | |
| agg ccc ggc tgg tac tgc gcg ctg agc aag cag gag ggg tgc cgg ctg | 497 |
| Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu | |
| 100 105 110 | |
| tgc gcg ccg ctg cgc aag tgc cgc ccg ggc ttc ggc gtg gcc aga cca | 545 |
| Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro | |
| 115 120 125 130 | |
| gga act gaa aca tca gac gtg gtg tgc aag ccc tgt gcc ccg ggg acg | 593 |
| Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr | |
| 135 140 145 | |
| ttc tcc aac acg act tca tcc acg gat att tgc agg ccc cac cag atc | 641 |
| Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile | |
| 150 155 160 | |
| tgt aac gtg gtg gcc atc cct ggg aat gca agc atg gat gca gtc tgc | 689 |
| Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys | |
| 165 170 175 | |
| acg tcc acg tcc ccc acc cgg agt atg gcc cca ggg gca gta cac tta | 737 |
| Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu | |
| 180 185 190 | |
| ccc cag cca gtg tcc aca cga tcc caa cac acg cag cca act cca gaa | 785 |
| Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu | |
| 195 200 205 210 | |
| ccc agc act gct cca agc acc tcc ttc ctg ctc cca atg ggc ccc agc | 833 |
| Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser | |
| 215 220 225 | |

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| | |
|---|------|
| ccc cca gct gaa ggg agc act ggc gac ttc gct ctt cca gtt gga ctg | 881 |
| Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu | |
| 230 235 240 | |
| att gtg ggt gtg aca gcc ttg ggt cta cta ata ata gga gtg gtg aac | 929 |
| Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn | |
| 245 250 255 | |
| tgt gtc atc atg acc cag gtg aaa aag aag ccc ttg tgc ctg cag aga | 977 |
| Cys Val Ile Met Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg | |
| 260 265 270 | |
| gaa gcc aag gtg cct cac ttg cct gcc gat aag gcc cgg ggt aca cag | 1025 |
| Glu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln | |
| 275 280 285 290 | |
| ggc ccc gag cag cag cac ctg ctg atc aca gcg ccg agc tcc agc agc | 1073 |
| Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser | |
| 295 300 305 | |
| agc tcc ctg gag agc tcg gcc agt gcg ttg gac aga agg gcg ccc act | 1121 |
| Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala Pro Thr | |
| 310 315 320 | |
| cgg aac cag cca cag gca cca ggc gtg gag gcc agt ggg gcc ggg gag | 1169 |
| Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly Glu | |
| 325 330 335 | |
| gcc cgg gcc agc acc ggg agc tca gat tct tcc cct ggt ggc cat ggg | 1217 |
| Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly | |
| 340 345 350 | |
| acc cag gtc aat gtc acc tgc atc gtg aac gtc tgt agc agc tct gac | 1265 |
| Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp | |
| 355 360 365 370 | |
| cac agc tca cag tgc tcc tcc caa gcc agc tcc aca atg gga gac aca | 1313 |
| His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr | |
| 375 380 385 | |
| gat tcc agc ccc tcg gag tcc ccg aag gac gag cag gtc ccc ttc tcc | 1361 |
| Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser | |
| 390 395 400 | |
| aag gag gaa tgt gcc ttt cgg tca cag ctg gag acg cca gag acc ctg | 1409 |
| Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu | |
| 405 410 415 | |

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 Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala
 420 425 430

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 Gly Met Lys Pro Ser
 435 440

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09902176 071001

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| Met | Ala | Pro | Val | Ala | Val | Trp | Ala | Ala | Leu | Ala | Val | Gly | Leu | Glu | Leu |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |
| Trp | Ala | Ala | Ala | His | Ala | Leu | Pro | Ala | Gln | Val | Ala | Phe | Thr | Pro | Tyr |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Ala | Pro | Glu | Pro | Gly | Ser | Thr | Cys | Arg | Leu | Arg | Glu | Tyr | Tyr | Asp | Gln |
| | | 35 | | | | | 40 | | | | | 45 | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Ala | Gln | Met | Cys | Cys | Ser | Lys | Cys | Ser | Pro | Gly | Gln | His | Ala | Lys |
| 50 | | | | | | 55 | | | | | 60 | | | | |
| Val | Phe | Cys | Thr | Lys | Thr | Ser | Asp | Thr | Val | Cys | Asp | Ser | Cys | Glu | Asp |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Ser | Thr | Tyr | Thr | Gln | Leu | Trp | Asn | Trp | Val | Pro | Glu | Cys | Leu | Ser | Cys |
| | | | | 85 | | | | | 90 | | | | | | 95 |
| Gly | Ser | Arg | Cys | Ser | Ser | Asp | Gln | Val | Glu | Thr | Gln | Ala | Cys | Thr | Arg |
| | | | 100 | | | | | 105 | | | | | | 110 | |
| Glu | Gln | Asn | Arg | Ile | Cys | Thr | Cys | Arg | Pro | Gly | Trp | Tyr | Cys | Ala | Leu |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Ser | Lys | Gln | Glu | Gly | Cys | Arg | Leu | Cys | Ala | Pro | Leu | Arg | Lys | Cys | Arg |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Pro | Gly | Phe | Gly | Val | Ala | Arg | Pro | Gly | Thr | Glu | Thr | Ser | Asp | Val | Val |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Cys | Lys | Pro | Cys | Ala | Pro | Gly | Thr | Phe | Ser | Asn | Thr | Thr | Ser | Ser | Thr |
| | | | | 165 | | | | | 170 | | | | | | 175 |
| Asp | Ile | Cys | Arg | Pro | His | Gln | Ile | Cys | Asn | Val | Val | Ala | Ile | Pro | Gly |
| | | | 180 | | | | | 185 | | | | | | 190 | |
| Asn | Ala | Ser | Met | Asp | Ala | Val | Cys | Thr | Ser | Thr | Ser | Pro | Thr | Arg | Ser |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Met | Ala | Pro | Gly | Ala | Val | His | Leu | Pro | Gln | Pro | Val | Ser | Thr | Arg | Ser |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Gln | His | Thr | Gln | Pro | Thr | Pro | Glu | Pro | Ser | Thr | Ala | Pro | Ser | Thr | Ser |
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| Phe | Leu | Leu | Pro | Met | Gly | Pro | Ser | Pro | Pro | Ala | Glu | Gly | Ser | Thr | Gly |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Asp | Phe | Ala | Leu | Pro | Val | Gly | Leu | Ile | Val | Gly | Val | Thr | Ala | Leu | Gly |
| | | | 260 | | | | 265 | | | | | | 270 | | |
| Leu | Leu | Ile | Ile | Gly | Val | Val | Asn | Cys | Val | Ile | Met | Thr | Gln | Val | Lys |
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| Lys | Lys | Pro | Leu | Cys | Leu | Gln | Arg | Glu | Ala | Lys | Val | Pro | His | Leu | Pro |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Ala | Asp | Lys | Ala | Arg | Gly | Thr | Gln | Gly | Pro | Glu | Gln | Gln | His | Leu | Leu |
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| Ile | Thr | Ala | Pro | Ser | Ser | Ser | Ser | Ser | Ser | Leu | Glu | Ser | Ser | Ala | Ser |
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| Ala | Ser | Ser | Thr | Met | Gly | Asp | Thr | Asp | Ser | Ser | Pro | Ser | Glu | Ser | Pro |
| | | | | 405 | | | | | 410 | | | | | 415 | |
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 Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
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 Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp
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Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro
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245 250 255

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| Glu | Ala | Lys | Val | Pro | His | Leu | Pro | Ala | Asp | Lys | Ala | Arg | Gly | Thr | Gln | | |
| 275 | | | | | 280 | | | | | 285 | | | | | 290 | | |
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| ggc | ccc | gag | cag | cag | cac | ctg | ctg | atc | aca | gcg | ccg | agc | tcc | agc | agc | 1073 | |
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| Ser | Ser | Leu | Glu | Ser | Ser | Ala | Ser | Ala | Leu | Asp | Arg | Arg | Ala | Pro | Thr | | |
| | | | 310 | | | | | | 315 | | | | | 320 | | | |
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| cgg | aac | cag | cca | cag | gca | cca | ggc | gtg | gag | gcc | agt | ggg | gcc | ggg | gag | 1169 | |
| Arg | Asn | Gln | Pro | Gln | Ala | Pro | Gly | Val | Glu | Ala | Ser | Gly | Ala | Gly | Glu | | |
| | | 325 | | | | | 330 | | | | | 335 | | | | | |
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| | | 340 | | | | 345 | | | | | 350 | | | | | | |
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| acc | cag | gtc | aat | gtc | acc | tgc | atc | gtg | aac | gtc | tgt | agc | agc | tct | gac | 1265 | |
| Thr | Gln | Val | Asn | Val | Thr | Cys | Ile | Val | Asn | Val | Cys | Ser | Ser | Ser | Asp | | |
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| cac | agc | tca | cag | tgc | tcc | tcc | caa | gcc | agc | tcc | aca | atg | gga | gac | aca | 1313 | |
| His | Ser | Ser | Gln | Cys | Ser | Ser | Gln | Ala | Ser | Ser | Thr | Met | Gly | Asp | Thr | | |
| | | | 375 | | | | | | 380 | | | | | 385 | | | |
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| gat | tcc | agc | ccc | tcg | gag | tcc | ccg | aag | gac | gag | cag | gtc | ccc | ttc | tcc | 1361 | |
| Asp | Ser | Ser | Pro | Ser | Glu | Ser | Pro | Lys | Asp | Glu | Gln | Val | Pro | Phe | Ser | | |
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| | | | | | | | | | | | | | | | | | |
| aag | gag | gaa | tgt | gcc | ttt | cgg | tca | cag | ctg | gag | acg | cca | gag | acc | ctg | 1409 | |
| Lys | Glu | Glu | Cys | Ala | Phe | Arg | Ser | Gln | Leu | Glu | Thr | Pro | Glu | Thr | Leu | | |
| | | 405 | | | | | 410 | | | | | 415 | | | | | |
| | | | | | | | | | | | | | | | | | |
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| Leu | Gly | Ser | Thr | Glu | Glu | Lys | Pro | Leu | Pro | Leu | Gly | Val | Pro | Asp | Ala | | |
| | | 420 | | | | 425 | | | | | 430 | | | | | | |
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| Gly | Met | Lys | Pro | Ser | | | | | | | | | | | | | |
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 Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
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 Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
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 Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
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 Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
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 Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
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| | | | | | | | | | | | | | | | | | | |
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| Ser | Lys | Gln | Glu | Gly | Cys | Arg | Leu | Cys | Ala | Pro | Leu | Arg | Lys | Cys | Arg | 130 | 135 | 140 |
| Pro | Gly | Phe | Gly | Val | Ala | Arg | Pro | Gly | Thr | Glu | Thr | Ser | Asp | Val | Val | 145 | 150 | 155 |
| Cys | Lys | Pro | Cys | Ala | Pro | Gly | Thr | Phe | Ser | Asn | Thr | Thr | Ser | Ser | Thr | 165 | 170 | 175 |
| Asp | Ile | Cys | Arg | Pro | His | Gln | Ile | Cys | Asn | Val | Val | Ala | Ile | Pro | Gly | 180 | 185 | 190 |
| Asn | Ala | Ser | Met | Asp | Ala | Val | Cys | Thr | Ser | Thr | Ser | Pro | Thr | Arg | Ser | 195 | 200 | 205 |
| Met | Ala | Pro | Gly | Ala | Val | His | Leu | Pro | Gln | Pro | Val | Ser | Thr | Arg | Ser | 210 | 215 | 220 |
| Gln | His | Thr | Gln | Pro | Thr | Pro | Glu | Pro | Ser | Thr | Ala | Pro | Ser | Thr | Ser | 225 | 230 | 235 |
| Phe | Leu | Leu | Pro | Met | Gly | Pro | Ser | Pro | Pro | Ala | Glu | Gly | Ser | Thr | Gly | 245 | 250 | 255 |
| Asp | Phe | Ala | Leu | Pro | Val | Gly | Leu | Ile | Val | Gly | Val | Thr | Ala | Leu | Gly | 260 | 265 | 270 |
| Leu | Leu | Ile | Ile | Gly | Val | Val | Asn | Cys | Val | Ile | Met | Thr | Gln | Val | Lys | 275 | 280 | 285 |
| Lys | Lys | Pro | Leu | Cys | Leu | Gln | Arg | Glu | Ala | Lys | Val | Pro | His | Leu | Pro | 290 | 295 | 300 |
| Ala | Asp | Lys | Ala | Arg | Gly | Thr | Gln | Gly | Pro | Glu | Gln | Gln | His | Leu | Leu | 305 | 310 | 315 |
| Ile | Thr | Ala | Pro | Ser | Ser | Ser | Ser | Ser | Ser | Ser | Leu | Glu | Ser | Ser | Ala | 325 | 330 | 335 |
| Ala | Leu | Asp | Arg | Arg | Ala | Pro | Thr | Arg | Asn | Gln | Pro | Gln | Ala | Pro | Gly | 340 | 345 | 350 |
| Val | Glu | Ala | Ser | Gly | Ala | Gly | Glu | Ala | Arg | Ala | Ser | Thr | Gly | Ser | Ser | 355 | 360 | 365 |
| Asp | Ser | Ser | Pro | Gly | Gly | His | Gly | Thr | Gln | Val | Asn | Val | Thr | Cys | Ile | 370 | 375 | 380 |
| Val | Asn | Val | Cys | Ser | Ser | Ser | Asp | His | Ser | Ser | Gln | Cys | Ser | Ser | Gln | 385 | 390 | 395 |
| Ala | Ser | Ser | Thr | Met | Gly | Asp | Thr | Asp | Ser | Ser | Pro | Ser | Glu | Ser | Pro | 405 | 410 | 415 |
| Lys | Asp | Glu | Gln | Val | Pro | Phe | Ser | Lys | Glu | Glu | Cys | Ala | Phe | Arg | Ser | 420 | 425 | 430 |
| Gln | Leu | Glu | Thr | Pro | Glu | Thr | Leu | Leu | Gly | Ser | Thr | Glu | Glu | Lys | Pro | 435 | 440 | 445 |
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Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
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Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp
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Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn
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